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Dedicated to Prof. Dr. Roberto A. Rossi on the occasion of his 60th anniversary

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Abstract

New 2-chloromethyl-6-halogeno-imidazo[1,2-*a*]pyridines and 2-chloromethyl-6-halogeno-3-nitroimidazo[1,2-*a*]pyridines were prepared and reacted under experimental conditions of $S_{RN}1$ reactions with different sulfur and carbon centered nucleophiles to give new 6-halogeno-2-substituted-imidazo[1,2-*a*]pyridines and 6-halogeno-3-nitro-2-substituted-imidazo[1,2-*a*] pyridines in good yields. Only the chloromethyl group was found to be reactive under these experimental conditions.

Keywords: Imidazo[1,2-*a*]pyridine, reductive alkylating agent, nitroheterocycles, $S_{RN}1$

Introduction

Substitution reactions at an sp^3 carbon atom of the reductive alkylating agents, *p*-nitrobenzyl chloride or 2-halogeno-2-nitropropane, which proceed via a chain multi-stage sequence involving radical anions and free radicals as intermediates were first proposed independently by Kornblum[1] and Russell[2] in 1966. This pathway has been applied in 1970 to rationalize the substitution of unactivated aromatic halides and named $S_{RN}1$ by Bunnett.[3] The process has a considerably wide scope and synthetic capabilities. Recently, all the aspects of nucleophilic substitution reactions by electron transfer have been magnificently reviewed by Rossi, Pierini and Peñéñory.[4] Among the heterocyclic analogues of *o*-nitrobenzyl derivatives which react by $S_{RN}1$ reactions, our group has reported the $S_{RN}1$ reactions of nitronate anions with a series of imidazoles fused to a heterocyclic ring bearing the chloromethyl group *ortho* to the nitro group.

This system constitue a powerful synthetic tool to obtain nitro heterocycles with potential pharmaceutical properties.[5]

Imidazo[1,2-*a*]pyridine derivatives are important compounds which are known for their useful pharmacological activities.[6] For example, gastric antisecretory,[7] local anesthetic,[8] antiviral,[9] hypnotic[10] and antianxiety[11] properties have been described. The nature and the position of the substituent on the pyridinic moiety influence these activities.[9] Zolpidem (Stilnox®, Ambien®, Myslee®) saled by Sanofi-Synthélabo, is a non-benzodiazepine hypnotic of the imidazopyridine class, leader of the international market with a blockbuster status for the treatment of sleep disorders.

As part of our current interest on the synthesis by $S_{RN}1$ reactions of new imidazo[1,2-*a*]pyridines, which can be used in different coupling reactions for the preparation of more complex structures of pharmacological interest, we have prepared new 2-chloromethyl-6-halogeno-imidazo[1,2-*a*]pyridines **3a-b** and 2-chloromethyl-6-halogeno-3-nitroimidazo[1,2-*a*]pyridines **4a-b** (Figure 1) and studied their reactivity with different nucleophiles under $S_{RN}1$ experimental conditions.

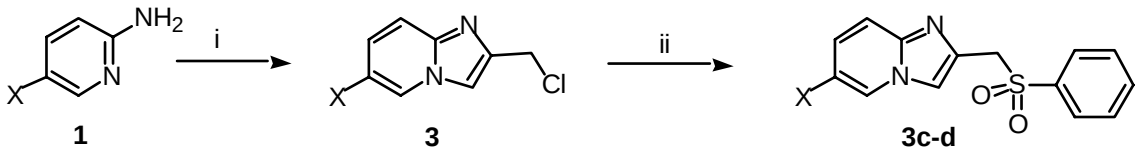
Figure 1. 2-Chloromethyl-6-halogeno-imidazo[1,2-*a*]pyridines and 2-chloromethyl-6-halogeno-3-nitro-imidazo[1,2-*a*]pyridines.

Results and Discussion

Herein we describe the synthesis of **3a** and **3b** (Scheme 1) starting respectively from the commercially available 2-amino-5-chloropyridine (**1a**) or 2-amino-5-bromopyridine (**1b**) by condensation with 1,3-dichloroacetone (**2)** and nitration to give **4a** and **4b** (Scheme 2) and their conversion to new 6-halogeno-2-substituted-imidazo[1,2-*a*]pyridines **3c-d** by reaction with sodium benzenesulfinate (Scheme 1) and 6-halogeno-3-nitro-2-substituted-imidazo[1,2-*a*] pyridines by $S_{RN}1$ reactions with lithium salt of 2-nitropropane **5a-b** (Scheme 2), sodium phenylthiolate **6a-b,** sodium benzenesulfinate **7a-b** and sodium salt of diethylmalonate **8a-b** (Scheme 3).

Although $S_{RN}1$ displacements of aromatic substrates by sulfur nucleophiles can be achieved in DMSO with different types of initiation,[3] the $PhSO_2^-$ anion has not been reported to react. With photostimulation in DMSO in presence of 2 equivalents of the sodium salt of benzenesulfinic acid, **3a** and **3b** react probably following an S_N2 mechanism only at the

chloromethyl group with good yield, respectively 69 and 80%, to give the corresponding sulfones **3c** and **3d**. No substitution of chloride or bromide in position 6 has been observed under these experimental conditions. The sulfones **3c** and **3d** were also obtained with similar yields without photostimulation.

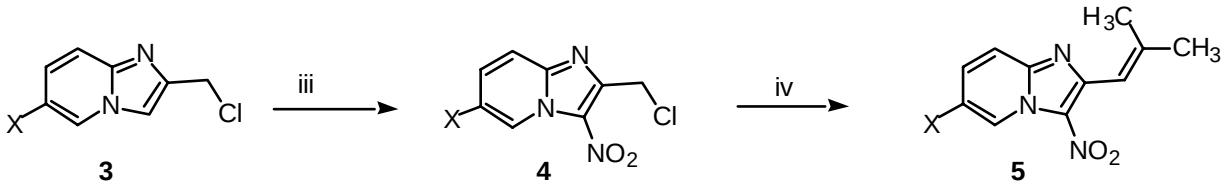


1 **3** **3c-d**

1a, X = Cl; **1b**, X = Br **3a**, X = Cl; **3b**, X = Br **3c**, X = Cl; **3d**, X = Br

Scheme 1. Reagents and conditions: (i) $ClCH_2COCH_2Cl$ (**2**), EtOH, reflux, 6 h; (ii) $C_6H_5SO_2Na$, DMSO, N_2, hν, 3 h.

The $S_{RN}1$ displacements on the pyridine moiety of the imidazo[1,2-*a*]pyridine being more difficult than an S_N2 on the chloromethyl group, we have prepared, new reductive alkylating agents, the nitro derivatives **4a** and **4b** and studied their conversion with different nucleophiles to the corresponding derivatives by $S_{RN}1$ reactions at the sp^3 carbon atom of the chloromethyl group.



3 **4** **5**

3a, X = Cl; **3b**, X = Br **4a**, X = Cl; **4b**, X = Br **5a**, X = Cl; **5b**, X = Br

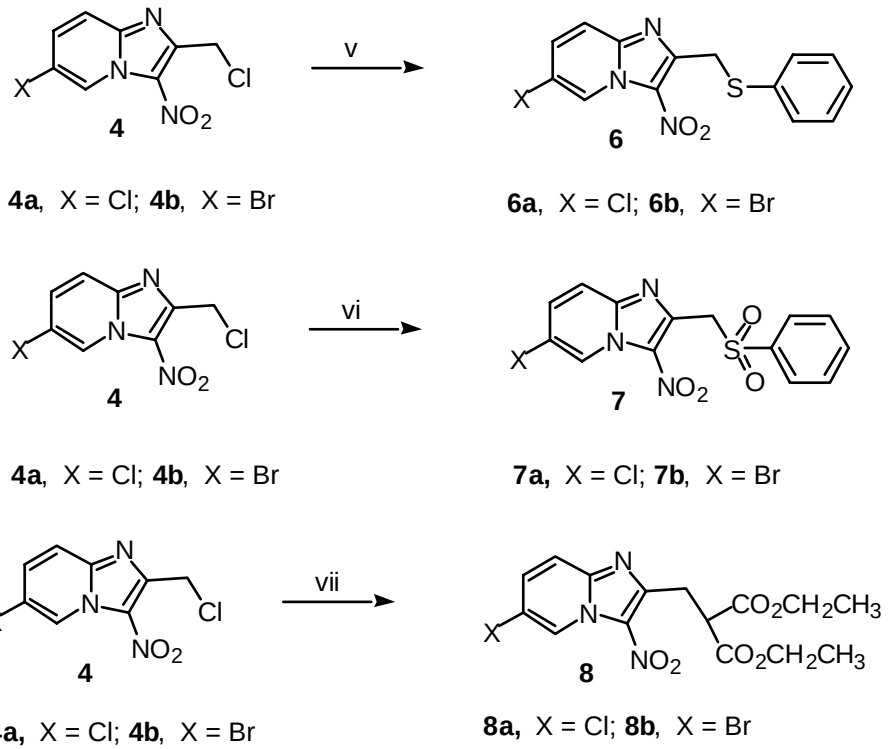
Scheme 2. Reagents and conditions: (iii) H_2SO_4, HNO_3 60%, 0 °C to RT 3 h. (iv) $LiCNO_2(CH_3)_2$, DMSO, N_2, hν, 0.3 h.

The *C*-alkylation of 2-nitropropane anion, which is a classical example of an $S_{RN}1$ reaction at sp^3 carbon atom of an *o*- or *p*-nitrobenzyl chloride, gives with **4a** and **4b** (Scheme 2) the ethylenic derivatives **5a** and **5b** in 70% yields. **5a** and **5b** result of the consecutive *C*-alkylation of the 2-nitropropane anion and nitrous acid elimination from the *C*-alkylation product (Scheme 2). These reactions are strongly inhibited in presence of TEMPO, a classical free scavenger used in the mechanism studies of $S_{RN}1$ reactions.[12]

With the phenylthiolate anion, **4a** and **4b** react to give the corresponding sulfides **6a** and **6b** in 80% yields. (Scheme 3). These reactions also are inhibited in presence of TEMPO.

With the phenylsulfinate anion, **4a** and **4b** react to give the corresponding sulfones **7a** and **7b** in 80% yields. These sulfones could be used for further $S_{RN}1$ reactions with different electrophiles as recently shown in nitroimidazole series.[13]

Finally, **4a** and **4b** react with diethyl malonate anion to give the corresponding diethyl malonates in 85% yields. Further functional group transformations could give lactams of pharmaceutical interest.[14]



Scheme 3. Reagents and conditions: (v) NaH 60%, HSC_6H_5, DMSO, 1 h and N_2, hν, 0.5 h. (vi) $C_6H_5SO_2Na$, DMSO, N_2, 3 h, hν. (vii) $CH_2(CO_2CH_2CH_3)_2$, DMSO, NaH 60%, 0.5 h and N_2, hν, 2 h.

In conclusion, the 2-chloromethyl-6-halogeno-imidazo[1,2-*a*]pyridines **3a-b** and 2-chloromethyl-6-halogeno-3-nitroimidazo[1,2-*a*]pyridines **4a-b** react with different sulfur or carbon centered anions only by substitution of the chloromethyl group. The reactions with 2-chloromethyl-6-halogeno-3-nitroimidazo[1,2-*a*]pyridines **4a-b** are very probably $S_{RN}1$ reactions. These new 6-halogeno-imidazo[1,2-*a*]pyridines could be used in different coupling reactions for the preparation of more complex structures of pharmacological interest. Work is in progress to prepare new derivatives by the Suzuki reaction and $S_{RN}1$ reaction on the pyridine moiety.

Experimental Section

General Procedures. Melting points were determined with a B-540 Büchi melting point apparatus. 300 MHz ^{1}H NMR and 75.4 MHz ^{13}C NMR spectra were recorded on a Bruker Avance DPX 300 in $CDCl_3$ or DMSO-d_6 solution at the Centre Régional de RMN de la Faculté des Sciences et Techniques de Saint-Jérôme. ^{1}H and ^{13}C NMR chemical shifts (δ) are reported in ppm with respect to $CHCl_3$ 7.26 ppm (^{1}H) and 77.16 ppm (^{13}C) or DMSO 2.62 ppm (^{1}H) and 40.6 ppm (^{13}C). The multiplicity of the signals is: s, singulet; d, doublet; t, triplet; q, quadruplet; m, multiplet. Elemental analyses were carried out at the Centre de Microanalyses de la Faculté des Sciences et Techniques de Saint-Jérôme.

6-Chloro-2-chloromethylimidazo[1,2-*a*]pyridine (3a). To a solution of 1,3-dichloroacetone (**2**) (2.17 g, 0.0171 mol, 1.1 eq) in absolute ethanol (24 mL) was added 2 g (0.0155 mol, 1 eq) of 2-amino-5-chloropyridine (**1a**). The mixture was stirred and heated under reflux for 6 h. The solvent was evaporated *in vacuo* and the residue was taken up in H_2O (50 mL) and basified with saturated aqueous solution of Na_2CO_3. The solution was extracted with $CHCl_3$ (3 x 80 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated *in vacuo.* Flash column chromatography of the crude solid on silica gel (solvent Et_2O) yielded **3a** (62%) as a light brown solid. The analytical sample of **3a** was obtained as a light brown solid by crystallization (isopropanol), m.p. 127.4 °C. ^{1}H NMR ($CDCl_3$) δ 4.74 (s, 2H, CH_2); 7.15 (dd, *J* = 2.0 Hz, *J* = 9.6 Hz, 1H, H_7); 7.50 (d, *J* = 9.6 Hz, 1H, H_8); 7.58 (s, 1H, H_3); 8.12 (dd, *J* = 0.9 Hz, *J* = 2.0 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 39.3 (CH_2); 111.2 (CH); 118.1 (CH); 120.9 (C); 123.5 (CH); 126.6 (CH); 143.7 (C); 144.2 (C). Anal. Calcd. for $C_8H_6Cl_2N_2$: C, 47.79; H, 3.01; N, 13.93. Found: C, 47.69; H, 3.01; N, 14.05.

6-Bromo-2-chloromethylimidazo[1,2-*a*]pyridine (3b). **Caution: this compound is a skin irritant.** Following the procedure used for **3a**. Flash column chromatography of the crude solid on silica gel (solvent $CHCl_3$/AcOEt 9:1) afforded **3b** (58%) as a white solid from **1b** and **2**. The analytical sample of **3b** was obtained as a white solid by crystallization (isopropanol), m.p. 127.7 °C. ^{1}H NMR ($CDCl_3$) δ 4.73 (s, 2H, CH_2); 7.22 (dd, *J* = 2.0 Hz, *J* = 9.5 Hz, 1H, H_7); 7.45 (dd, *J* = 9.5 Hz, 1H, H_8); 7.57 (s, 1H, H_3); 8.22 (dd, *J* = 1.0 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 39.3 (CH_2); 107.4 (C); 111.0 (CH); 118.3 (CH); 125.8 (CH); 128.7 (CH); 143.9 (C). The quaternary carbon atom bearing bromo group was not observed under these experimental conditions. Anal. Calcd. for $C_8H_6BrClN_2$: C, 39.14; H, 2.46; N, 11.41. Found: C, 39.13; H, 2.42; N, 11.36.

2-Benzenesulfonylmethyl-6-chloroimidazo[1,2-*a*]pyridine (3c).[15] To a solution of sodium benzenesulfinate (1.64 g, 10 mmol, 2 eq) in DMSO (40 mL) under an inert atmosphere (N_2) and irradiation with a tungsten 150W lamp was added 1 g (5.0 mmol, 1 eq) of 6-chloro-2-chloromethylimidazo[1,2-*a*]pyridine (**3a**). The mixture was stirred at room temperature for 3 h. After disappearance of **3a** (monitored by TLC), the mixture was poured into an ice-water mixture and a solid precipitated. The white solid was collected by filtration and dried in the air to

give **3c** in 69% yield. The analytical sample of **3c** was obtained as a white solid by crystallization (isopropanol), m.p. 178.7 °C. ^{1}H NMR ($CDCl_3$) δ 4.57 (s, 2H, CH_2); 7.11 (dd, *J* = 2.0 Hz, *J* = 9.6 Hz, 1H, H_7); 7.30-7.80 (m, 7H); 8.12 (dd, *J* = 0.5 Hz, *J* = 2.0 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 56.3 (CH_2); 113.4 (CH); 117.9 (CH); 121.1 (C); 123.4 (CH); 126.4 (CH); 128.3 (CH*2); 129.1 (CH*2); 133.8 (CH); 135.0 (C); 138.6 (C); 143.3 (C). Anal. Calcd. for $C_{14}H_{11}ClN_2O_2S$: C, 54.81; H, 3.61; N, 9.13. Found: C, 54.85; H, 3.64; N, 9.21.

2-Benzenesulfonylmethyl-6-bromoimidazo[1,2-*a*]pyridine (3d). Following the procedure used for **3c**, the bromo derivative **3d** was obtained as a white-grey solid in 80% yield from sodium benzenesulfinate and **3b**. The analytical sample of **3d** was obtained as a white-grey solid by crystallization (isopropanol), m.p. 216.4 °C. ^{1}H NMR (DMSO-d_6) δ 4.83 (s, 2H, CH_2); 7.31-7.83 (m, 8H); 8.91 (s, 1H). ^{13}C NMR (DMSO-d_6) δ 55.7 (CH_2); 114.1 (CH); 117.9 (CH); 127.1 (CH); 128.0 (CH); 128.1 (CH*2); 129.3 (CH*2); 134.0 (C); 135.0 (C); 139.0 (CH); 142.7 (C). Anal. Calcd. for $C_{14}H_{11}BrN_2O_2S$: C, 47.88; H, 3.16; N, 7.98. Found: C, 47.88; H, 3.24; N, 7.95.

6-Chloro-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (4a). To a solution of (**3a**) (1.40 g, 7 mmol, 1 eq) in concentrated sulfuric acid (14 mL, 25.8 g, 0.26 mol, 37 eq) cooled by an ice-water bath, nitric acid 65% (1.4 mL, 1.9 g, 0.02 mol, 2.9 eq) was added. The mixture was stirred and allowed to warm to room temperature and stirred at room temperature for 3 h. The mixture was poured into an ice-water mixture and a solid precipitated. The yellow solid was collected by filtration and dried in the air to give **4a** in 70% yield. The analytical sample of **4a** was obtained as a yellow solid by crystallization (isopropanol), m.p. 198.1 °C. ^{1}H RMN ($CDCl_3$) δ 5.10 (s, 2H, CH_2); 7.65 (dd, *J* = 2.0 Hz, *J* = 9.5 Hz, 1H, H_7); 7.80 (dd, *J* = 0.7 Hz, *J* = 9.5 Hz, 1H, H_8); 9.50 (dd, *J* = 0.7 Hz, *J* = 2.0 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 38.6 (CH_2); 118.9 (CH); 125.7 (C); 125.9 (CH); 132.3 (CH); 143.0 (C); 147.9 (C). The quaternary carbon atom bearing nitro group was not observed under these experimental conditions. Anal. Calcd. for $C_8H_5Cl_2N_3O_2$: C, 39.05; H, 2.05; N, 17.08. Found: C, 39.18; H, 1.99; N, 17.12.

6-Bromo-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (4b). Following the procedure used for **4a**, the bromo derivative **4b** was obtained as a yellow solid in 100% yield from **3b**. The analytical sample of **4b** was obtained as a yellow solid by crystallization (isopropanol), m.p. 205.6 °C. ^{1}H NMR (DMSO-d_6) δ 5.12 (s, 2H, CH_2); 7.96 (dd, *J* = 0.8 Hz, *J* = 9.4 Hz, 1H, H_8); 8.03 (dd, *J* = 1.7 Hz, *J* = 9.4 Hz, 1H, H_7); 9.42 (dd, *J* = 0.8 Hz, *J* = 1.7 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 38.6 (CH_2); 112.4 (C); 119.1 (CH); 127.7 (CH); 134.6 (CH); 143.1 (C); 147.7 (C). The quaternary carbon atom bearing nitro group was not observed under these experimental conditions. Anal. Calcd. for $C_8H_5BrClN_3O_2$: C, 33.08; H, 1.73; N, 14.66 Found: C, 33.14; H, 1.65; N, 14.54.

6-Chloro-2-(2-methylpropenyl)-3-nitroimidazo[1,2-*a*]pyridine (5a). To a solution of lithium salt of 2-nitropropane (0.465 g, 4.9 mmol, 3 eq) in DMSO (15 mL) under an inert atmosphere (N_2) and irradiation with a tungsten 150W lamp was added 0.4 g (1.63 mmol, 1 eq) of 6-chloro-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (**4a**). The mixture was stirred at room temperature for 20 minutes. After disappearance of **4a** (monitored by TLC) , the mixture was poured into an ice-water mixture and extracted with diethyl ether (3 x 80 mL). The combined organic phases

were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give **5a** as a orange solid. Purification by column chromatography (silica gel), eluting with a mixture of chloroform-diethyl ether (8/2) gave **5a** in 70% yield. The analytical sample of **5a** was obtained as a pale orange solid by crystallization (isopropanol), m.p. 133.8 °C. ^{1}H NMR ($CDCl_3$) δ 2.10 (d, *J* = 1.1 Hz, 3H, CH_3); 2.33 (d, *J* = 1.1 Hz, 3H, CH_3); 7.06 (septuplet, *J* = 1.1 Hz, 1H, CH); 7.52 (dd, *J* = 1.8 Hz, *J* = 9.4 Hz, 1H, H_7); 7.68 (dd, *J* = 0.4 Hz, *J* = 9.4 Hz, 1H, H_8); 9.53 (dd, *J* = 0.4 Hz, *J* = 1.8 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3); 28.3 (CH_3); 115.2 (CH); 117.9 (CH); 124.1 (C); 125.9 (CH); 131.8 (CH); 143.5 (C); 149.2 (C); 151.2 (C). Anal. Calcd. for $C_{11}H_{10}ClN_3O_2$: C, 52.50; H, 4.01; N, 16.70. Found: C, 52.64; H, 4.00; N, 16.64.

6-Bromo-2-(2-methylpropenyl)-3-nitroimidazo[1,2-*a*]pyridine (5b). Following the procedure used for **5a**, the bromo derivative **5b** was obtained as a yellow solid in 70% yield from **4b**. The analytical sample of **5b** was obtained as a yellow solid by crystallization (isopropanol), m.p. 132 °C. ^{1}H NMR ($CDCl_3$) δ 2.08 (d, *J* = 1.1 Hz, 3H, CH_3); 2.32 (d, *J* = 1.1 Hz, 3H, CH_3); 7.05 (septuplet, *J* = 1.1 Hz, 1H, CH); 7.60 (dd, *J* = 0.9 Hz, *J* = 9.4 Hz, 1H, H_8); 7.66 (dd, *J* = 1.8 Hz, *J* = 9.4 Hz, 1H, H_7); 9.61 (dd, *J* = 0.9 Hz, *J* = 1.8 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3); 28.3 (CH_3); 110.5 (C); 115.2 (CH); 118.1 (CH); 127.9 (CH); 134.0 (CH); 143.6 (C); 148.9 (C); 151.3 (C). Anal. Calcd. for $C_{11}H_{10}BrN_3O_2$: C, 44.62; H, 3.40; N, 14.14. Found: C, 44.56; H, 3.46; N, 14.32.

6-Chloro-3-nitro-2-phenylsulfanylmethylimidazo[1,2-*a*]pyridine (6a). Sodium hydride 60% (0.32 g, 13.6 mmol, 3.3 eq) and thiophenol (1.34 g, 12.2 mmol, 3 eq) under an inert atmosphere (N_2) were added to DMSO (50 mL). The mixture was stirred for 1 h and 1 g (4.08 mmol, 1 eq) of 6-chloro-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (**4a**) was added. The mixture was stirred at room temperature for 30 minutes under irradiation with a tungsten 150W lamp. After disappearance of **4a** (monitored by TLC) , the mixture was poured into an ice-water mixture and a solid precipitated. The yellow solid was filtered and dried in the air to give **6a** in 80% yield. The analytical sample of **6a** was obtained as a yellow solid by crystallization (isopropanol), m.p. 172.9 °C. ^{1}H NMR ($CDCl_3$) δ 4.66 (s, 2H, CH_2); 7.19-7.52 (m, 5H); 7.60 (dd, *J* = 2.0 Hz, *J* = 9.4 Hz, 1H, H_7); 7.70 (dd, *J* = 0.8 Hz, *J* = 9.4 Hz, 1H, H_8); 9.49 (dd, *J* = 0.8 Hz, *J* = 2.0 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 33.2 (CH_2); 118.3 (CH); 125.1 (C); 125.7 (CH); 126,9 (CH); 128.9 (CH*2); 130.3 (CH*2); 132.0 (CH); 135.0 (C); 143.0 (C); 150.3 (C). Anal. Calcd. for $C_{14}H_{10}ClN_3O_2S$: C, 52.59; H, 3.15; N, 13.14. Found: C, 52.43; H, 3.14; N, 13.15.

6-Bromo-3-nitro-2-phenylsulfanylmethylimidazo [1,2-*a*] pyridine (6b). Following the procedure used for **6a**, the bromo derivative **6b** was obtained as a yellow solid in 80% yield from **4b**. The analytical sample of **6b** was obtained as a yellow solid by crystallization (isopropanol), m.p. 173 °C. 1H NMR ($CDCl_3$) δ 4.66 (s, 2H, CH_2); 7.19-7.70 (m, 7H); 9.58 (dd, *J* = 1.1 Hz, *J* = 1.6 Hz, 1H, H5). ^{13}C NMR ($CDCl_3$) δ 33.3 (CH_2); 111.7 (C); 118.6 (CH); 126.9 (CH); 127.8 (CH); 128.9 (CH*2); 130.4 (CH*2); 134.2 (CH); 135.0 (C); 143.1 (C); 150.2 (C). The quaternary carbon atom bearing nitro group was not observed under these experimental conditions. Anal. Calcd. for C14H10BrN3O2S: C, 46.17; H, 2.77; N, 11.54. Found: C, 46.22; H, 2.61; N, 11.50.

2-Benzenesulfonylmethyl-6-chloro-3-nitroimidazo[1,2-*a*]pyridine (7a). To a solution of 1.34 g (8.2 mmol, 2 eq) of sodium benzenesulfinate in DMSO (50 mL) under an inert atmosphere was added 1 g (4.1 mmol, 1 eq) of 6-chloro-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (**4a**). The mixture was stirred at room temperature for 3 h under irradiation with a tungsten 150W lamp. After disappearance of **4a** (monitored by TLC), the mixture was poured into an ice-water mixture and a solid precipitated. The yellow solid was filtered and dried in the air to give **7a** in 80% yield. The analytical sample of **7a** was obtained as a pale beige solid by crystallization (isopropanol), m.p. 219.2 °C. ^{1}H NMR ($CDCl_3$), δ 5.12 (s, 2H, CH_2); 7.50-7.90 (m, 7H); 9.43 (dd, *J* = 0.8 Hz, *J* = 1.9 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 56.7 (CH_2); 118.9 (CH); 125.6 (CH); 125.9 (C); 128.3 (CH*2); 129.3 (CH*2); 132.3 (CH); 134.2 (CH); 139.1 (C); 139.7 (C); 143.2 (C). The quaternary carbon atom bearing nitro group was not observed under these experimental conditions. Anal. Calcd. for $C_{14}H_{10}ClN_3O_4S$: C, 47.80; H, 2.87; N, 11.95. Found: C, 47.75; H, 2.84; N, 12.01.

2-Benzenesulfonylmethyl-6-bromo-3-nitroimidazo[1,2-*a*]pyridine (7b). Following the procedure used for **7a**, the bromo derivative **7b** was obtained as a yellow solid in 80% yield from **4b**. The analytical sample of **7b** was obtained as a yellow solid by crystallization (isopropanol), m.p. 237.7 °C. ^{1}H NMR ($CDCl_3$) δ 5.14 (s, 2H, CH_2); 7.28-7.90 (m, 7H); 9.54 (s, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 56.6 (CH_2); 112.5 (C); 119.1 (CH); 127.6 (CH); 128.3 (CH*2); 129.3 (CH*2); 134.3 (CH); 134.6 (CH); 139.0 (C); 139.5 (C); 143.3 (C). The quaternary carbon atom bearing nitro group was not observed under these experimental conditions. Anal. Calcd. for $C_{14}H_{10}BrN_3O_4S$: C, 42.44; H, 2.54; N, 10.61. Found: C, 42.58; H, 2.46; N, 10.55.

Diethyl 2-(6-chloro-3-nitroimidazo[1,2-*a*]pyridin-2-ylmethyl)malonate (8a). Sodium hydride 60% (0.54 g, 13.5 mmol, 3.3 eq) and diethyl malonate (1.3 g, 12.2 mmol, 3 eq) under an inert atmosphere (N_2) were added to DMSO (20 mL). The mixture was stirred 0.5 h and 1 g (4.08 mmol, 1 eq) of 6-chloro-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (**4a**) was added. The mixture was stirred at room temperature for 2 h under irradiation with a tungsten 150W lamp. After disappearance of **4a** (monitored by TLC), the mixture was poured into an ice-water mixture and a solid precipitated. The pale beige solid was collected by filtrationf and dried in the air to give **8a** in 85% yield. The analytical sample of **8a** was obtained as a pale beige solid by crystallization (isopropanol), m.p. 143 °C. ^{1}H NMR ($CDCl_3$) δ 1.27 (t, *J* = 7.2 Hz, 6H, 2*CH_3); 3.83 (d, *J* = 7.2 Hz, 2H, CH_2); 3.57 (m, 5H, 2* CH_2, CH); 7.57 (dd, *J* = 2.0 Hz, *J* = 9.5 Hz, 1H, H_7); 7.66 (dd, *J* = 0.8 Hz, *J* = 9.5 Hz, 1H, H_8); 9.50 (dd, *J* = 0.8 Hz, *J* = 2.0 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 14.0 (2*CH_3); 29.4 (CH_2); 49.3 (CH); 61.7 (2* CH_2); 118.2 (CH); 124.9 (C); 125.7 (CH); 131.8 (CH); 143.0 (C); 150.9 (C); 168.6 (C). Anal. Calcd. for $C_{15}H_{16}ClN_3O_6$: C, 48.72; H, 4.36; N, 11.36. Found: C, 48.76; H, 4.36; N, 11.36.

Diethyl 2-(6-bromo-3-nitroimidazo[1,2-*a*]pyridin-2-ylmethyl)malonate (8b). Following the procedure used for **8a**, the bromo derivative **8b** was obtained as a pink beige solid in 85% yield from **4b**. The analytical sample of **8b** was obtained as a pink beige solid by crystallization (isopropanol), m.p. 141 °C. ^{1}H NMR (DMSO-d_6) δ 1.17 (t , *J* = 7.1 Hz, 6H, 2*CH_3); 3.66 (d, *J* = 7.4 Hz, 2H, CH_2); 4.15 (t, *J* = 7.4 Hz, 1H, CH); 4.15 (q, *J* = 7.1 Hz, 4H, 2*CH_2); 7.86 (dd, *J* =

9.4 Hz, 1H, H_8); 7.97 (dd, *J* = 1.8 Hz, *J* = 9.4 Hz, 1H, H_7); 9.42 (d, *J* = 1.0 Hz, 1H, H_5). ^{13}C NMR ($CDCl_3$) δ 14.0 (2*CH_3); 29.4 (CH_2); 49.4 (CH); 61.7 (2* CH_2); 111.4 (C); 118.4 (CH); 127.8 (CH); 134.0 (CH); 150.8 (C); 168.7 (C). Anal. Calcd. for $C_{15}H_{16}BrN_3O_6$: C, 43.50; H, 3.89; N, 10.14. Found: C, 43.39; H, 3.93; N, 10.26.

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